Session 3.4
Policy implementation

Lecture

Status and perspectives of alternative testing methods for chemical safety assessment in the regulatory context

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The marketing and use of chemicals for various purposes require hazard and risk assessment with respect to human health and the environment. Depending on the respective legal context specific information including data on (eco)toxicological properties is required in order to perform hazard and risk assessment. For mutual acceptance of data reasons internationally standardised and accepted testing methods are required. The majority of testing methods in toxicology – and to a certain extent in ecotoxicology – involve testing with vertebrate animals. For animal welfare reasons the OECD has committed to the 3R principle already 1982, simultaneously encouraging to discover, develop and validate alternative testing systems. In recent years a number of *in vitro* test methods have been developed, validated and published as OECD test guidelines, many of them with the engagement of the German ZEBET. Especially with the new European Chemicals Policy REACH, which aims at improved environmental and human health safety without additional animal testing wherever possible, the development of alternative testing methods and "intelligent testing strategies" including also QSARs is of utmost importance.

Poster

A critical analysis of the 2002 EU statistics on the use of laboratory animals for scientific purposes

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The European Commission (EC) recently published its fourth report on the number of animals used in the EU. Although, a set of standardised tables are now used, the new reporting format still fails to provide an adequate level of information regarding the use of laboratory animals. The reports are only published every three years. As such there may be a tendency to ensure that fewer animals are used, or reported as being used, in those years. Further underestimates of animal use within the 15 Member States arise from the exclusion of animal breeding for, for instance, the generation of transgenic strains rather than for direct experimentation. Neither do the statistics indicate whether the animals used were normal, genetically modified or contain harmful genetic defects, which is especially relevant given that mouse transgenics research has persistently increased over the past decade. The UK statistics include animals used in breeding programs and in transgenic experimentation such that the UK domestic statistics report almost 1 million more animals than appeared in the UK submission to the EU statistics. Further discrepancies will be discussed, but it is clear that changes are required to improve the way in which statistics on laboratory animals in the EU are reported. This will allow trends to be discovered more readily and areas for reduction, refinement and replacement initiatives to be identified.

Lecture

Three years of animal welfare in the German Constitution – the balance from an animal welfare perspective

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The inclusion of animal welfare into the German Constitution in 2002 gained world-wide attention. With great expectations animal welfare organisations had been lobbying and campaigning to reach this goal for more than a decade, and they had good reasons to do so: in several concrete cases the regulations of the German Animal Welfare Act had been overruled by basic rights laid down in the Constitution, such as the freedom of science, the freedom of education and the freedom of professional choice. According to a decision of the German Federal Constitutional Court, licensing authorities were not allowed to reject applications for animal experiments on scientific or ethical grounds.

Three years after the change in the Constitution has taken place not much seems to have changed concerning the practice of animal experimentation, and the regulation thereof, in Germany. Therefore, it is time for a review of the situation. This presentation looks at case studies from different areas of research involving animals to analyse which consequences the change of Constitution actually has brought about. Licensing procedures as well as specific cases of animal husbandry and care are examined. Also, findings of a survey among licensing authorities and members of ethics committees undertaken in 2005 are used to assess the practical implications of the change in the German legislation.

This review is to yield a list of concrete measures that would need to be taken by the government and the authorities to pay regard to the animal welfare requirements resulting from the amended Constitution.

Lecture

Botulinum testing – time to kill the LD_{50}

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The classic LD_{50} test, developed in 1927, has, since the end of the 1970s, been widely criticised for both scientific and animal welfare reasons. In 2002 the original LD_{50} test (OECD 401) was deleted from the OECD guidelines, and replaced by modified versions of the LD_{50}, requiring fewer animals. These are: the fixed dose procedure (TG 420), acute toxic class method (TG 423) and the up-and-down procedure (TG 425).

One of the few remaining instances where the classic LD_{50} is still used today is the mouse LD_{50} test, in the potency and safety testing of botulinum toxin, used in both cosmetic and therapeutic preparations.

The European Pharmacopoeia has set the regulatory framework for non-animal testing of botulinum toxin type A for injection (No. 2113; 5th edition EP). A non-animal immunoassay – the SNAP-25 endopeptidase assay – has shown excellent results with respect to the estimation of the potency of type A toxin in therapeutic preparations (*ATLA 31*, 381-391, 2003). Similarly, two rapid, non-animal assays have also been developed for botulinum toxin type B.

The only remaining obstacle to regulatory approval of these non-animal methods would appear to be the validation process. There is a moral imperative to give priority to the validation process with respect to these particular non-animal methods in view of the fact that this test requires over 80,000 mice in the UK alone every year.

Lecture

Strategies to reduce animal testing in US EPA's HPV program

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The High Production Volume (HPV) program was launched in the US by the EPA in 1998. In an effort to reduce the number of animals killed in this large testing initiative, members of the animal welfare community met with government officials and negotiated several basic principles set forth in a letter from EPA to all HPV participants (10/14/99), and reiterated in a Federal Register notice. The goal was to avoid check-the-box toxicology in fulfilling the basic SIDS data set, which if followed for each chemical, would result in well over a million animal deaths. Laudable goals included the formation of chemical categories, the use of existing data to the greatest extent possible, and similar common sense approaches to spare animals and still meet the goals of the program. After more than five years experience and review of over 370 test plans, the success of this effort is disappointing. Many examples exist in which companies duplicated testing, for example, if the data were non GLP. In other instances, published data existed which were not used, either individually or in conjunction with other data (in a weight of evidence approach) to avoid new animal testing. Over time, however, some successful strategies were developed by reviewers in the animal welfare community and in collaboration with conscientious companies to reduce testing and still meet the SIDS requirements. Examples of these strategies will be provided and explored as they might apply to future testing programs.

Lecture

Access to obfuscation: Can rigid confidentiality and public accountability co-exist?

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In many industrialised countries, it can be nearly impossible for a member of the public to obtain current and specific information regarding animal experiments. In Canada, research protocols specifying the number and species of animals used in an experiment, the procedures to which they were subjected, and the associated level of invasiveness, are considered "confidential," as are meeting minutes of institutional animal care committees and reports of government inspections and private accreditations. The public does not even have access to a complete list of laboratories that conduct animal experiments. British policy is even more restrictive, such that it is a criminal offense to release such information publicly. Relatively greater transparency exists under U.S. "freedom of information" legislation, notwithstanding gaps in federal oversight and documentation for the most commonly used, yet "unregulated," species. In contrast, the Swedish constitution guarantees the right of every citizen to have access to documents held by public authorities, which many Swedes consider to be an indispensable part of the democratic process. Legislated and other mechanisms enabling public access to official documents concerning animal experiments in these four countries will be examined, as will arguments both for and against preserving the confidential nature of certain types of research information. Overarching policy questions that will be explored include: "What level and type of information does the public need to make an informed decision about the need for and acceptability of animal experiments?" and, "Can rigid confidentiality and public accountability truly co-exist in a democratic society?"

Lecture

LD_{50} Testing of Botox® Cosmetic

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Using animals for testing products with a cosmetic purpose has been controversial for decades. As revealed in a 2003 exposé by FRAME, the potency testing of Botox® Cosmetic, the popular wrinkle smoother, currently entails not only animal use for a cosmetic purpose, but also uses one of the most heavily criticised animal-based tests, namely, the LD_{50} test. Consequently, we argue that the manufacturer of Botox Cosmetic – Allergan, Inc. – has an ethical obligation to expeditiously replace the LD_{50} test with a non-animal method and, in the meantime, institute any appropriate reduction and refinement alternatives. The Humane Society of the United States (HSUS) approached the US-based company in 2004 to request disclosure of the details of its potency testing of Botox Cosmetic and its efforts at replacement, reduction, and refinement. Allergan revealed few details, and also declined an HSUS offer to work with the company to move this issue forward. The competent US authorities, the Food and Drug Administration (FDA), claim that they "encourage" alternative methods of assessing the potency of Botox Cosmetic, but do not appear to be doing anything concrete to move the issue forward. Some form of potency testing of Botox Cosmetic is essential, given that its active ingredient, botulinum toxin, is one of the deadliest substances known to man. Potential Three Rs alternatives have been identified by the European Pharmacopeia. Whatever alternatives are developed and validated for Botox Cosmetic will also apply to its sister product, Botox, which has several therapeutic applications.